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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,913	01/20/2004	Neil Moss	9/216-1-D1	4313

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EXAMINER	
HUYNH, CARLIC K	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
12/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,913	MOSS ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on October 2, 2007 is acknowledged.

Status of the Claims

Claims 1-4 and 6-23 are pending and are considered herewith. It in noted that in an "Amendment – After Non-Final Rejection" filed on October 2, 2007, Applicants have amended claims 1, 15-16, and 20 to treatment of "cytokine-mediated cancer". Accordingly, claims 1-4 and 6-23 are being examined on the merits herein.

Response to Arguments

1. Applicants' amendment, see "Amendment – After Non-Final Rejection" filed on October 2, 2007, with respect to "Specification" to the Objection to the Specification for having a non-descriptive title has fully considered and is found persuasive. Examiner had objected to the instant title, "Methods of Treating Cancer", for being too general. Applicants have amended the instant title to "Methods of Treating Cytokine-Mediated Cancer with Heterocyclic Aromatic Compounds". Examiner accepts the amended title. Thus, the Objection to the Specification for having a non-descriptive title has been withdrawn in light of the amendment.

2. Applicants' amendment, see "Amendment – After Non-Final Rejection" filed on October 2, 2007, with respect to "Remarks/Arguments" to Rejections under 35 U.S.C. § 112, first paragraph has been fully considered and is found persuasive. Examiner had objected to claims 1-4 and 6-23 as not being enabled for any cancer or tumor other than those mediated by cytokines. Applicants have amended claims 1-4 and 6-23 to "cytokine-mediated cancer". Thus

the Rejections under 35 U.S.C. § 112, first paragraph to claims 1-4 and 6-23 have been withdrawn in light of the amendments.

3. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on October 2, 2007, with respect to "Remarks/Arguments" to Rejections under 35 U.S.C. § 103(a) to claim 1 have been fully considered and are persuasive. Applicants have argued that Kapadia et al. (US 6,492,529) and the current application (10/761,913) were, at the time the current invention was made, owned by Boehringer-Ingelheim Corporation. Examiner agrees and Kapadia is not available as a reference under 35 U.S.C. § 103(a). Thus, the Rejections under 35 U.S.C. § 103 to claims 1-4 and 6-23 have been withdrawn in light of the arguments.

4. Applicant's amendments, see "Amendment-After Non-Final Rejection" filed on October 2, 2007, with respect to "Remarks/Arguments" to Obviousness Type Double Patenting Rejections to claims 1, 20, and 22 as well as to claims 1, 12-14, 16, and 20-23 have been fully considered and are persuasive. Examiner had rejected claims 1, 20, and 22 over claims 14 and 16 of Cirillo et al. (US 6,319,921), over claims 11 and 13 of Cirillo et al. (US 6,329,415), over claims 23-25 of Breitfelder et al. (US 6,358,945), over claims 12, 14, and 16 of Regan (US 6,372,773), and over claim 19 of Cirillo et al. (US 6,825,184). Moreover, Examiner had rejected claims 1, 12-14, 16, and 20-23 over claims 1 and 5-6 of Cirillo et al. (US 6,333,325), over claims 3 and 5 of Cirillo et al. (US 6,525,046), and over claims 1, 11-13, and 17 of Moss et al. (US 6,916,814). Examiner acknowledges the correction of US 6,825,184 to US 6,916,814. Applicants have filed terminal disclaimers for the following patents: 6,525,046; 6,825,184; 6,333,325; 6,329,415; 6,372,773; 6,916,814; 6,319,921; and 6,358,945. The terminal disclaimers were filed on October 2, 2007 and were approved on October 12, 2007. Thus, the

Obviousness Type Double Patenting Rejections to claims 1, 20 and 22 and to claims 1, 12-14, 16, and 20-23 have been withdrawn in light of the amendments.

5. Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection. The following new ground(s) of rejection to new claim 2 is used herewith.

6. It is noted that the compounds of formula (I), namely 1-[5-(2-hydroxy-1,1-dimethyl-ethyl)-2-p-tolyl-2H-pyazol-3-yl]-3-[4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl]-urea and 1-[5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl]-3-[4-(2-morpholin-4-yl-ethoxy)naphthalene-1-yl]-urea, have been found to be free of the prior art. Thus, a more general search of compounds of formula (I) is used herewith.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-4 and 6-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dumas et al. (WO 99/32110 as cited in the IDS) in view of Hanna (US 2002/0012665), Bruserud (Leukemia Research, 1996, Vol. 20, No. 1, pp. 65-73), and Treon et al. (Current Opinion in Hematology, 1998, Vol. 5, pp. 42-48).

Dumas et al. teach a method of treating cytokine mediated diseases in humans or mammals comprising administering a group of aryl ureas, which are the compounds of formula (I) and pharmaceutically acceptable salts of formula (I) (abstract; page 6, lines 26-27; and page 15, lines 1-2). The compounds of formula (I) are useful for a number of cytokine mediated disease including cancer (page 7, lines 17 and 19).

Dumas et al. do not explicitly teach genotoxic therapy and treatment for multiple myeloma and acute myelogenous leukemia blasts.

Hanna teaches a method for treating hematologic malignancies comprising administrating cytokine antagonists in combination with chemotherapy drugs (abstract and page 3, paragraph [0026]). Hematologic malignancies include acute myelogenous leukemia (page 3, paragraph [0030]). Thus it would be obvious that Hanna teaches a method of treating acute myelogenous leukemia. Chemotherapy drugs include alkylating agents (page 10, paragraph [0094]). Moreover, Hanna discloses that a "cytokine antagonist" may be an interleukin (page 6, paragraph [0058]).

Bruserud teaches that inhibition of interleukin 1 (IL1) causes the blockade of acute myelogenous leukemia blast proliferation (page 72). Since IL1 is a cytokine antagonist and since inhibition of IL1 blocks acute myelogenous leukemia blast proliferation, it would be obvious that acute myelogenous leukemia is a cytokine mediated cancer.

Treon et al. teach that interleukin-6 (IL-6) is a key growth factor for multiple myeloma cells and that drugs that interfere with IL-6 signaling have a role in the treatment of multiple myeloma (abstract and page 42). Since IL-6 is a cytokine antagonist and IL-6 is a key growth factor for multiple myeloma cells, it would be obvious that multiple myeloma is a cytokine mediated cancer.

To a person of skill in the art at the time of the invention, it would have been obvious to employ the compounds of formula (I) of Dumas et al. to treat cytokine mediated cancers such as multiple myeloma and acute myelogenous leukemia because the compounds of Hanna, Bruserud, and Treon et al. are used for treating various cancers and tumors including multiple myeloma and acute myelogenous leukemia and according to Hanna and Bruserud, cytokine antagonists can be used to treat cytokine mediated cancers such as acute myelogenous leukemia and according to Treon et al., cytokine antagonists can be used to treat cytokine mediated cancers such as multiple myeloma.

The motivation to combine the compounds of Dumas et al. to the compounds of Hanna, Bruserud and Treon et al. is that the compounds of Hanna, Bruserud, and Treon et al. are used for treating cytokine mediated cancers such as acute myelogenous leukemia and multiple myeloma.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Regarding genotoxic therapy as recited in instant claim 15, it is also noted that "genotoxic therapy" is well known in the art to be a compound capable of binding DNA and causing a mutation and it is also noted that "alkylating agents" are well known in the art to be compounds that bind to DNA by an alkyl group. Hanna teaches a method for treating hematologic malignancies comprising administrating cytokine antagonists in combination with chemotherapy drugs which include alkylating agents (abstract; page 3, paragraph [0026]); and page 10, paragraph [0094]). Thus it is obvious to one skilled in the art that alkylating agents can be used for genotoxic therapy because they bind to DNA.

Conclusion

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ckh